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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/577,657	05/25/2000	Misako Mizuno	029430-454	6902

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EXAMINER

KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 05/03/2002

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/577,657

Applicant(s)

MIZUNO ET AL.

Examiner

Anne Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-10, 13-17 and 20-28 is/are pending in the application.
- 4a) Of the above claim(s) 8-10, 15 and 24-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 1-7, 13, 14, 16, 17, 20-23, 27 and 28 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. The cancellation of claims 11-12 and 18-19, the amendment of claims 1-7, 13-14, 16-17 and 20-23, and the addition of new claims 26-28 requested in Paper No. 15, filed 19 February, 2002, have been entered. Claims 1-10, 13-17 and 20-28 are pending.

2. Newly submitted claim 26 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 26 is drawn to a protein, which belongs to Group III, as indicated in the restriction requirement of 23 July, 2001.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 26 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Accordingly, claims 8-10, 15 and 24-26 are withdrawn from consideration as being drawn to nonelected inventions. Claims 1-7, 13-14, 16-17, 20-23 and 27-28 are examined.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

5. The substitute specification filed 19 February, 2002, has not been entered because there was no marked-up copy showing the amendments made via the substitute specification relative to the specification at the time the substitute specification was filed.

Response to Amendment

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6. The rejection of claims 1-6 and 11-12 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is WITHDRAWN in light of amendments to the claims to indicate that the DNAs and RNAs are isolated.

7. The rejection of claims 1-2, 4-5, 7, 11-14 and 16-23 under 35 U.S.C. 102(e) as being anticipated by Stiles et al is WITHDRAWN given the amendment to the claims to more clearly indicate that the modified nucleic acid encodes an enzyme with the same activities as SEQ ID NO:1 and given the data showing that the enzyme of the instant invention does not possess xanthosine-N7-methyl transferase activity (response pg 18-20).

Claim Objections

8. Claims 1, 4, 14, 17, 20-21 and 27 are objected to because of the following informalities:

Claims 1 and 4 have an improper article before "polypeptide" in line 7.

Claim 14 lacks an article before "N-methyl" in line 2.

There is an improper article at the start of claims 17 and 23.

In claims 20-21, line 4, "coffea" should be capitalized.

Claim 27 has an improper article before "RNA".

9. Claim 14 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The vector of claim 14 already encodes an N-methyl transferase. If Applicant intended that the vector express the enzyme in a microorganism of plant, the claim should be so amended.

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Claim Rejections - 35 USC § 112

10. Claims 1-2, 4-5, 7, 13-14, 16-17, 20-23 and 27-28 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids of SEQ ID NO:2 and plant cells and plants transformed with those nucleic acids, does not reasonably provide enablement for nucleic acids that encode SEQ ID NO:1, encode modified nucleic acids or that hybridize under unspecified stringency to nucleic acids that encode SEQ ID NO:1, as stated in the prior Office action for claims 1-2, 4-5, 7, 11-14 and 16-23. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's arguments filed 19 February, 2002 have been fully considered but they are not persuasive. Applicant urges that it is within the ability of one of skill in the art to produce modified nucleic acids that encode proteins with the recited enzymatic activities (response, pg 9).

This is not found persuasive because the specification fails to teach which amino acids are critical for protein function and which are not and can thus be altered. Making all possible single amino acid substitutions in a 356 amino acid long protein like that encoded by SEQ ID NO:2 would require making and analyzing 19^{356} nucleic acids. Because nucleic acids that hybridize to nucleic acids that encode SEQ ID NO:2 or that encode variants of SEQ ID NO:2 would have many more than a single substitution, nucleic acids with many more substitutions would need to be made and analyzed. As the specification does not provide guidance for this nucleic acid modification, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims, if such nucleic acids are even obtainable.

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In addition, as discussed in the prior Office action, SEQ ID NO:1 does not appear to be the entire protein sequence. Kato et al (2000, Nature 406 956-957) teach a gene encoding a caffeine synthase that is identical to the caffeine synthase of the instant invention except the published enzyme is 13 amino acids longer at its N-terminal (see sequence search results). All experiments involving transformation used a DNA comprising SEQ ID NO:2, which is almost identical to the nucleic acid taught by Kato et al and would encode the full-length enzyme.

There is no evidence to suggest that a nucleic acid encoding only SEQ ID NO:1 would function to encode an enzyme with the listed properties, especially since the starting ATG is missing.

11. Claims 20-23 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, as stated in the prior Office action for claims 18-23.

Applicant's arguments filed 19 February, 2002 have been fully considered but they are not persuasive. Applicant urges that claims 20-23 have been amended limit the plant tissue to camellia or coffee (response pg 10).

This is not found persuasive because given the unpredictability associated with antisense suppression of genes that are not completely homologous to the target gene as detailed in the prior Office action, it is not certain that such a gene will inhibit sense gene transcription or secondary metabolite levels when transformed into a plant of a different species.

The instant specification does not teach production of ANY plant metabolite. As discussed in the prior Office action, alteration of secondary metabolites is unpredictable.

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Additionally, transformation with a gene that encodes one enzyme is unlikely to alter the production of any nonspecified secondary metabolite in the plant.

The claims are also drawn to a method for changing the "composition" of any plant secondary metabolite (versus changing profile, ratio, or concentration). The instant specification provides no guidance for altering the "composition" of any plant metabolite, including caffeine or caffeine precursors.

Applicant is invited to submit a declaration presenting data that demonstrates that the levels of caffeine in *Camellia* or the levels of any other plant secondary metabolite in *Camellia* or *Coffea* were altered by transformation with the nucleic acid of SEQ ID NO:2.

12. Claims 1-2, 4-5, 7, 13-14, 16-17, 20-23 and 27-28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, as stated in the prior Office action for claims 1-2, 4-5, 7, 11-14 and 16-23.

Applicant's arguments filed 19 February, 2002 have been fully considered but they are not persuasive. Applicant urges that it is within the ability of one of skill in the art to produce modified nucleic acids that encode proteins with the recited enzymatic activities (response, pg 10-11).

This is not found persuasive because the specification fails to describe the structural features of these modified nucleic acids. Description of one sequence does not adequately describe a multitude of sequences. See *In re Shokal*, 113 USPQ 283, (CCPA 1957) at pg 285

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; *In re Wahlforss et al.*, 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number

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of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary. ...

We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

13. Claims 1-7, 13-14, 16-17, 20-23 and 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention, as stated in the prior Office action for claims 1-7, 11-14 and 16-23 and for the new reasons indicated below. Dependent claims are included in all rejections. Applicant's arguments filed 19 February, 2002 have been fully considered but they are not persuasive.

Claims 1 and 4 remain indefinite because it is not clear if the DNA or RNA comprises both or either parts (a) and (b). See also the rejection of dependent claims 2 and 5, below.

Claims 1(b) and 4(b) remain indefinite in their recitation of "obtained by carrying out nucleotide replacement, deletion, or insertion". Applicant urges that the claims recite that substitutions, deletions or insertions are made such that the enzyme maintains the three enzymatic activities (response, pg 12). This is not found persuasive because it is not clear which or how many nucleotides have been replaced or inserted.

Claims 1(b) and 4(b) lack antecedent basis for the limitation "said modified sequence".

Claims 1(b) and 4(b) lack antecedent basis for the limitation "said enzyme activities". It is also not clear what maintenance of an enzyme activity is.

Claims 2 and 5 are indefinite in their recitation of "hybridized at a ... to overnight". In response to a similar rejection, Applicant urges that Sambrook et al describes stringent

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conditions (response, pg 13). This is not found persuasive because the level of stringency remains unclear. Hybridization conditions - *e.g.*, salt concentrations - are not indicated in the claim and wash conditions and times are not mentioned at all.

Claims 2 and 5 are indefinite in their recitation of "said nucleotide sequence (a) and said nucleotide sequence (b)". Not only is there a lack of antecedent basis for this particular wording, but it makes it appear that the DNA or RNA molecule of the parent claim has both sequences (a) and (b).

Claim 7 lacks antecedent basis for the limitation "said N-methyl transferase encoded by the DNA molecule".

Claim 23 is indefinite in its recitation of "a transformed whole plant". As parent claim 20 makes no reference to a transformed whole plant, it is unclear where in the method of claim 20 a transformed whole plant is formed.

14. Claims 1-7, 13-14, 16-17, 20-23 and 27-28 are free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid encoding SEQ ID NO:1 or encoding a N-methyl transferase with 7-methylxanthine N3 methyl transferase, theobromine N1 methyl transferase and paraxanthine N3 methyl transferase activities.

Conclusion

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

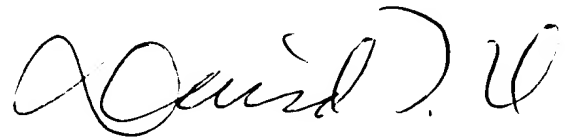
16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Kimberly Davis, at (703) 305-3015.

Anne R. Kubelik, Ph.D.
May 1, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180-1638

A handwritten signature in cursive script, appearing to read "David T. Fox", followed by a large, stylized "U" or checkmark-like flourish.